genzyme

GENZYME CORPORATION
ONE MOUNTAIN ROAD
P.O. BOX 9322
FRAMINGHAM, MA 01701-9322
508-872-8400
FAX 508-872-9080

March 13, 2000

The Dockets Management Branch (HFA-305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket # 00D-0186

To Whom It May Concern:

This letter provides Genzyme Corporation's comments on the initial components of a draft guidance document being developed under the auspices of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) entitled "M4 Common Technical Document", that was published in the Federal Register on February 11, 2000.

Genzyme appreciates the opportunity to comment on this proposed rule. Should you have any questions concerning these comments, please do not hesitate to call Betty Wiley or Alex Kuta, at 508-270-2132 and 508-270-2138, respectively.

Sincerely,

Betty Wiley, for

Alexander E. Kuta, Ph.D.
Senior Director
Regulatory Affairs
Genzyme Corporation

00D-0186

C3

Genzyme Corporation's Comments on M4 Common Technical Document

Module II-general

- With respect to the overall set up of the document, it would be helpful to include an overall introductory section to the document as is often done when filing a BLA or MAA. Module IIA begins with the Executive summaries in which introductory information is incorporated (to a limited extent). It may be helpful to set up guidelines for an overall introduction to the dossier to be provided for reviewers in Module IIA. IIB could then begin the Executive Summaries, and IIC and IID would follow with nonclinical and clinical summaries.

- Modules IIB and IIC will contain the summaries of nonclinical and clinical data. This format should be harmonized for regional differences and a guideline of what is expected (format, content etc) should be provided. Additionally it must be made clear whether these sections would replace the regional regulatory requirements of expert reports and/or Integrated Summaries of Safety and Efficacy.

Module IIB, Nonclinical summaries

- We believe the format for the nonclinical summaries should include an overall Executive Summary instead of separate Introductions and Summaries for each section (i.e. pharmacology, pharmacokinetics, toxicology & efficacy). A more efficient format would include an overall Executive Summary (10-12 pages) first, followed by individual study summaries (maximum of up to 100 pages). This revised format would be extremely beneficial to the reviewer in quickly getting the overall message for the pharm/tox section from first few pages of the document. Such a revised format could be also applied for other sections (CMC, Clinical).

- The Executive Summary should include highlights of the results obtained and conclusions backed up by a few Tables and Figures. The Tables should include study number, study design, results and conclusions.

- For nonclinical tabulated summaries, standard information should be included in each table, i.e., International Nonproprietary Name, title, report number, objective, study design, results, discussion, conclusions and location of technical report in CTD, etc. Recommendations to include these items were only listed on some of the table templates provided in the guideline.

- Figures and Tables should be incorporated within the text for ease of review.

- The across study/species summarization seems to be more appropriate in the executive summary section leaving the written summaries to a species by species discussion.

Module III (Quality) -General Comments

- The Expert Working Group (EWG) for the Quality module point out the difficulty of commenting on the document, at this time, by noting that the quality module section currently consists of a framework, i.e., table of contents, not a detailed breakdown of the requirements. Given the amount of effort that will be required by ICH to address the region specific requirements (pharmacopoeia harmonization, and level of detail expected in applications), when will the format become preferred, or required? If that date precedes harmonization of technical content, particularly level of detail, industry may realize little benefit from the exercise.

- The attachments promised for future reference, providing common requirements for the topics, are critical to properly evaluate the proposed document format.

- What commitment, if any, is there to evaluate codified regional requirements, which are beyond ICH's influence?

- While there is no commitment on behalf of the Quality EWG to address certain classes of pharmaceutical products, i.e., generics, OTC, the Clinical EWG has made some effort to do so. Is there a product type prioritization schedule? If so, what is it?

- Will the additional information provided as explanatory notes within the M4 document be equivalent to ICH guidance?

- Given that regional particulars will remain, another area that needs to be addressed to allow companies to submit essentially the same document to the regional authorities includes pharmacopoeia harmonization, which in turn impacts specification setting, choice of analytical procedures and their validation, and stability testing.

- Further items requiring consideration include the use of DMF files, which have more versatility in the US than in the EU and Japan, and the use of batch release criteria only in the EU. Also, batch requirements in the three regions vary substantially. Will any of these issues be addressed to truly harmonize the contents of the CTD?

- Will it be possible to generate a single Quality Executive Summary if the regional differences remain?

- Finally, efforts are focussed on providing common information to authorities. Efforts should also look at harmonizing the outcomes of the regulatory review process, such as labeling, specifications and post-marketing commitments.

- Suggest adding batch analysis to the Table of contents after section P4.3.

Module IV -General Comments

- The placement of a Table of All Studies in the Study Report section is confusing and is more appropriate in the summary section.

From: JUDITH A. BRILHANTE (508)270-2170
GENZYME CORPORATION
15 PLEASANT STREET CONNECTOR

FRAMINGHAM, MA, 01701

SHIPPER'S FEDEX ACCOUNT #

FedEx.

To: Dockets Management Branch (301)594-5476
(HFA-305)
5630 Fishers Lane
Room 1061
Rockville,, MD, 20852

SHIP DATE: 14MAR00
WEIGHT: 1 LBS

Ref: 7080-0000-3440-0990

DELIVERY ADDRESS
TRK # 7925 6106 6856 FORM 0201

PRIORITY OVERNIGHT

WED
AA
Deliver by:
15MAR00

20852-MD-US

IAD
ZM EDGA

Shipping Label

Schedule Courier | Find a Dropoff Location | Shipping History

Shipment Complete | Cancel Shipment

1. Use the "Print" feature from your browser to send this page to your laser printer.
2. Fold the printed page along the horizontal line.
3. Place label in air waybill pouch and affix it to your shipment so that the barcode portion of the label can be read and scanned.
4. To print a receipt of your shipment, please click on "Shipping History."

Ship a New Package

Ship Inside U.S. | Ship Outside U.S. | Ship to Same Recipient